

Applicants: Geoffrey P. DOBSON et al.
Serial No. 09/937,181

AMENDMENTS TO THE CLAIMS

Listing of Claims:

This listing of claims is to replace all previous listings.

77. (Currently Amended) A composition comprising:

a pharmaceutically acceptable carrier;

a compound chosen from a potassium channel opener, a potassium channel agonist and an adenosine receptor agonist; and

a local anesthetic;

wherein the compound and the local anesthetic are present in the composition in amounts sufficient to arrest the heart; and

wherein the pharmaceutically acceptable carrier includes potassium at a concentration of less than about 10mM.

78. (Previously Amended) The composition of claim 77, wherein the potassium channel opener or potassium channel agonist is selected from nicorandil, diazoxide, minoxidil, pinicadil, aprikalim, cromokulim, NS-1619 (1,3-dihydro-1-[2-hydroxy5(trifluoromethyl)phenyl]5-(trifluoromethyl)2-H-benzimidazol-one), amlodipine, Bay K 8644(L-type)(1,4-dihydro-26-dimethyl-5-nitro-4[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), bepridil HC1 (L-type), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIIC (Q-type), cyproheptadine HC1, dantrolene sodium (Ca^{2+} release inhibitor), diltiazem HC1 (L-type), flodipine, flunarizine HC1 ($\text{Ca}^{2+}/\text{Na}^{+}$), fluspirilene (L-type), HA-1077 2HC1(1-(5 isoquinoliny sulphonyl) homo piperazine.HC1), isradipine, loperamide HC1, manolide (Ca^{2+} release inhibitor), nicardipine HC1 (L-type), nifedipine (L-type), nifedipine HC1 (L-type), nimodipine (L-type), nitrendipine (L-type), pimozide (L- and T- type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HC1 (L-type), methoxy-verapamil HC1 (L-type), YS-035 HC1 (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-methyl benzene ethaneamine HC1) and AV blockers.

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79. (Currently Amended) The composition of claim 77, wherein the adenosine receptor agonist is selected from N⁶-cyclopentyladenosine (CPA), N-ethylcarboxamido adenosine (NECA), 2-[p-(2-carboxyethyl)phenethyl-amino-5'-N-ethylcarboxamido adenosine (CGS-21680), 2-chloroadenosine, N⁶-[2-(3,5-dimethoxyphenyl)-2-(2-methoxyphenyl)ethyladenosine, 2-chloro-N⁶-cyclopentyladenosine (CCPA), N-(4-aminobenzyl)-9-[5-(methylcarbonyl)-beta-D-ribofuranosyl]-adenine (AB-MECA), ([IS-[1a, 2b, 3b, 4a(S*)]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methyl-propyl]amino]-3H-imidazole[4,5-b]pyridyl-3-yl]cyclopentane carboxamide (AMP579, N⁶-(R)-phenylisopropyladenosine (R-PLA), aminophenylethyladenosine [9](APNEA) and cyclohexyladenosine (CHA).

80. (Previously Amended) The composition of claim 77, wherein the local anesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and Class 1B antiarrhythmic agents.

81. (Previously Amended) The composition of claim 80, wherein the Class 1B antiarrhythmic agents is lignocaine.

82. (Cancelled)

83. (Cancelled)

84. (Previously Amended) The composition of claim 77, wherein the pharmaceutically acceptable carrier comprises a buffer which maintains the pH of the composition in the range from about 6 to about 9.

85. (Cancelled)

86. (Cancelled)

87. (Previously Amended) The composition of claim 84, wherein the buffer

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is selected from the group consisting of Krebs-Henseleit, St. Thomas No. 2 solution, Tyrodes solution, Fremes solution, Hartmanns solution and Ringers-Lactate.

88. (Cancelled)

89. (Previously Amended) The composition of claim 77, wherein the pharmaceutically acceptable carrier comprises magnesium having a concentration of about 2.5 mM.

90. (Cancelled)

91. (Previously Amended) The composition of claim 77, further comprising a medicament chosen from dipyridamole and a clot-busting drug.

92. (Previously Presented) The composition of claim 91, wherein the clot-busting drug is streptokinase.

93. (Previously Presented) The composition of claim 78, wherein the AV blocker is adenosine.

94. (Currently Amended) A composition comprising:
a pharmaceutically acceptable carrier;
a compound chosen from a potassium channel opener, a potassium channel agonist and an adenosine receptor agonist; and
a local anesthetic;
wherein the compound and the local anesthetic are present in the composition in an amount sufficient to protect an organ;
wherein the pharmaceutically acceptable carrier includes potassium at a concentration of less than about 10mM.

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95. (Previously Presented) The composition of claim 94, wherein the potassium channel opener or potassium channel agonist is selected from nicorandil, diazoxide, minoxidil, pinicadil, aprikalim, cromokulim, NS-1619 (1,3-dihydro-1-[2-hydroxy5(trifluoromethyl) phenyl]5-(trifluoromethyl)2-H-benzimidazol-one), amlodipine, Bay K 8644(L-type)(1,4-dihydro-2,6-dimethyl-5-nitro-4[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), bepridil HC1 (L-type), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIIC (Q-type), cyproheptadine HC1, dantrolene sodium (Ca^{2+} release inhibitor), diltiazem HC1 (L-type), flodipine, flunarizine HC1 ($\text{Ca}^{2+}/\text{Na}^{+}$), fluspirilene (L-type), HA-1077 2HC1(1-(5 isoquinoliny sulphonyl) homo piperazine.HC1), isradipine, loperamide HC1, manolide (Ca^{2+} release inhibitor), nicardipine HC1 (L-type), nifedipine (L-type), niguldipine HC1 (L-type), nimodipine (L-type), nitrendipine (L-type), pmozide (L- and T- type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HC1 (L-type), methoxy-verapamil HC1 (L-type), YS-035 HC1 (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-methyl benzene ethaneamine HC1) and AV blockers.

96. (Currently Amended) The composition of claim 94, wherein the adenosine receptor agonist is selected from N^6 -cyclopentyladenosine (CPA), N-ethylcarboxamido adenosine (NECA), 2-[p-(2-carboxyethyl)phenethyl-amino-5'-N-ethylcarboxamido adenosine (CGS-21680),2-chloroadenosine, N^6 -[2-(3,5-dimethoxyphenyl)-2-(2-methoxyphenyl)ethyladenosine, 2-chloro- N^6 -cyclopentyladenosine (CCPA), N-(4-aminobenzyl)-9-[5-(methylcarbonyl)-beta-D-ribofuranosyl]-adenine (AB-MECA), ([IS-[1a, 2b, 3b, 4a(S*)]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methyl-propyl]amino]-3H-imidazole[4,5-b]pyridyl-3-yl]cyclopentane carboxamide (AMP579, N^6 -(R)-phenylisopropyladenosine (R-PLA), aminophenylethyladenosine [9](APNEA) and cyclohexyladenosine (CHA).

97. (Previously Presented) The composition of claim 94, wherein the local anesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and Class IB antiarrhythmic agents.

98. (Previously Presented) The composition of claim 97, wherein the Class

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1B antiarrhythmic agents is lignocaine.

99. (Previously Presented) The composition of claim 94, wherein the pharmaceutically acceptable carrier comprises a buffer which maintains the pH of the composition in the range from about 6 to about 9.

100. (Currently Amended) A composition comprising:
a pharmaceutically acceptable carrier;
a compound chosen from a potassium channel opener, a potassium channel agonist and an adenosine receptor agonist; and
a local anesthetic;
wherein the compound and the local anesthetic are present in the composition in an amount sufficient to preserve an organ, and
wherein the pharmaceutically acceptable carrier includes potassium at a concentration of less than about 10mM.

101. (Previously Presented) The composition of claim 100, wherein the potassium channel opener or potassium channel agonist is selected from nicorandil, diazoxide, minoxidil, pinicadil, aprikalim, cromokulim, NS-1619 (1,3-dihydro-1-[2-hydroxy5(trifluoromethyl) phenyl]5-(trifluoromethyl)2-H-benzimidazol-one), amlodipine, Bay K 8644(L-type)(1,4-dihydro-2,6-dimethyl-5-nitro-4[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), bepridil HC1 (L-type), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIC (Q-type), cyproheptadine HC1, dantrolene sodium (Ca^{2+} release inhibitor), diltiazem HC1 (L-type), flodipine, flunarizine HC1 ($\text{Ca}^{2+}/\text{Na}^{+}$), fluspirilene (L-type), HA-1077 2HC1(1-(5 isoquinoliny1 sulphonyl) homo piperazine.HC1), isradipine, loperamide HC1, manoalide (Ca^{2+} release inhibitor), nicardipine HC1 (L-type), nifedipine (L-type), niguldipine HC1 (L-type), nimodipine (L-type), nitrendipine (L-type), pimoziide (L- and T- type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HC1 (L-type), methoxy-verapamil HC1 (L-type), YS-035 HC1 (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-methyl benzene ethaneamine HC1) and AV blockers.

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102. (Currently Amended) The composition of claim 100, wherein the adenosine receptor agonist is selected from N⁶-cyclopentyladenosine (CPA), N-ethylcarboxamido adenosine (NECA), 2-[p-(2-carboxyethyl)phenethyl-amino-5'-N-ethylcarboxamido adenosine (CGS-21680), 2-chloroadenosine, N⁶-[2-(3,5-dimethoxyphenyl)-2-(2-methoxyphenyl)ethyladenosine, 2-chloro-N⁶-cyclopentyladenosine (CCPA), N-(4-aminobenzyl)-9-[5-(methylcarbonyl)-beta-D-ribofuranosyl]-adenine (AB-MECA), ([IS-[1a, 2b, 3b, 4a(S*)]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methyl-propyl]amino]-3H-imidazole[4,5-b]pyridyl-3-yl]cyclopentane carboxamide (AMP579, N⁶-(R)-phenylisopropyladenosine (R-PLA), aminophenylethyladenosine [9](APNEA) and cyclohexyladenosine (CHA).

103. (Previously Presented) The composition of claim 100, wherein the local anesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and Class 1B antiarrhythmic agents.

104. (Previously Presented) The composition of claim 100, wherein the Class 1B antiarrhythmic agents is lignocaine.

105. (Previously Presented) The composition of claim 100, wherein the composition is a cardioplegic or cardioprotectant composition.

106. (Previously Presented) The composition of claim 94, wherein the pharmaceutically acceptable carrier comprises a buffer which maintains the pH of the composition in the range from about 6 to about 9.

107. (New) The composition of claim 77, wherein the potassium channel opener or potassium channel agonist is selected from nicorandil, diazoxide, minoxidil, pinicadil, aprikalim, cromokulim, NS-1619 (1,3-dihydro-1-[2-hydroxy5(trifluoromethyl)phenyl]5-(trifluoromethyl)2-H-benzimidazol-one), amlodipine, Bay K 8644(L-type)(1,4-dihydro-2,6-dimethyl-5-nitro-4[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), bepridil HCl (L-type), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIC (Q-type), cyproheptadine HCl, dantrolene sodium (Ca²⁺ release inhibitor),

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diltiazem HC1 (L-type), filodipine, flunarizine HC1 ($\text{Ca}^{2+}/\text{Na}^+$), fluspirilene (L-type), HA-1077 2HC1(1-(5 isoquinoliny1 sulphonyl) homo piperazine.HC1), isradipine, loperamide HC1, manoalide (Ca^{2+} release inhibitor), nicardipine HC1 (L-type), niguldipine HC1 (L-type), nimodipine (L-type), nitrendipine (L-type), pimozide (L- and T- type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HC1 (L-type), methoxy-verapamil HC1 (L-type), YS-035 HC1 (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-methyl benzene ethaneamine HC1) and AV blockers.

108. (New) The composition of claim 94, wherein the potassium channel opener or potassium channel agonist is selected from nicorandil, diazoxide, minoxidil, pinicadil, aprikalim, cromokulim, NS-1619 (1,3-dihydro-1-[2-hydroxy5(trifluoromethyl) phenyl]5-(trifluoromethyl)2-H-benimidazol-one), amlodipine, Bay K 8644(L-type)(1,4-dihydro-26-dimethyl-5-nitro-4[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), bepridil HC1 (L-type), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIC (Q-type), cyproheptadine HC1, dantrolene sodium (Ca^{2+} release inhibitor), diltiazem HC1 (L-type), filodipine, flunarizine HC1 ($\text{Ca}^{2+}/\text{Na}^+$), fluspirilene (L-type), HA-1077 2HC1(1-(5 isoquinoliny1 sulphonyl) homo piperazine.HC1), isradipine, loperamide HC1, manoalide (Ca^{2+} release inhibitor), nicardipine HC1 (L-type), niguldipine HC1 (L-type), nimodipine (L-type), nitrendipine (L-type), pimozide (L- and T- type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HC1 (L-type), methoxy-verapamil HC1 (L-type), YS-035 HC1 (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-methyl benzene ethaneamine HC1) and AV blockers.

109. (New) The composition of claim 100, wherein the potassium channel opener or potassium channel agonist is selected from nicorandil, diazoxide, minoxidil, pinicadil, aprikalim, cromokulim, NS-1619 (1,3-dihydro-1-[2-hydroxy5(trifluoromethyl) phenyl]5-(trifluoromethyl)2-H-benimidazol-one), amlodipine, Bay K 8644(L-type)(1,4-dihydro-26-dimethyl-5-nitro-4[2(trifluoromethyl)phenyl]-3-pyridine carboxylic acid (methyl ester)), bepridil HC1 (L-type), calciseptine (L-type), omega-conotoxin GVIA (N-type), omega-conotoxin MVIIC (Q-type), cyproheptadine HC1, dantrolene sodium (Ca^{2+} release inhibitor), diltiazem HC1 (L-type), filodipine, flunarizine HC1 ($\text{Ca}^{2+}/\text{Na}^+$), fluspirilene (L-type), HA-

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1077 2HC1(1-(5 isoquinolinyl sulphonyl) homo piperazine.HCl), isradipine, loperamide HCl, manoalide (Ca^{2+} release inhibitor), nicardipine HCl (L-type), nifedipine HCl (L-type), nimodipine (L-type), nitrendipine (L-type), pimozide (L- and T- type), ruthenium red, ryanodine (SR channels), taicatoxin, verapamil HCl (L-type), methoxy-verapamil HCl (L-type), YS-035 HCl (L-type)N[2(3,4-dimethoxyphenyl)ethyl]-3,4-dimethoxy N-methyl benzene ethaneamine HCl) and AV blockers.

110. (New) A method of arresting a heart including the step of contacting the heart with a composition according to claim 77.

111. (New) A method of protecting an organ including the step of contacting the organ with a composition according to claim 94.

112. (New) A method of preserving an organ including the step of contacting the organ with a composition according to claim 100.